REMARKS

This Amendment is submitted in reply to the final Office Action mailed on May 31, 2007. A Request for Continued Examination (RCE) and petition for a one month extension of time submitted herewith. The Director is authorized to charge $790.00 for the RCE and $120.00 for one month extension of time and any additional fees that may be required, or to credit any overpayment to Deposit Account No. 02-1818. If such a withdrawal is made, please indicate the Attorney Docket No. 112713-983 on the account statement.

Claims 1-21 and 23-53 are currently pending in this application. Claims 22 and 54-120 were previously canceled. In the Office Action, Claims 1-21 and 23-53 are rejected under 35 U.S.C. §103. In response Claims 1, 19-20, 27-28, 32, 48 and 51 have been amended and Claims 2 and 12-18 have been canceled. These amendments do not add new matter. In view of the amendment and/or for the reasons set forth below, Applicants respectfully submit that the rejections should be withdrawn.

Claims 19-20, 27-28 and 32 have been amended for clarification purposes.

Claims 1-21, 23-35, and 48-53 are rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 5,935,847 to Smith et al. ("*Smith*") in view of U.S. Patent No. 6,759,245 to Toner et al. ("*Toner*"). Claims 36-47 are rejected under 35 U.S.C. § 103(a) as being unpatentable over *Smith* and *Toner* and in further view of U.S. Patent No. 5,989,215 to Delmotte ("*Delmotte*"). Applicants respectfully disagree with and traverse these alleged rejections for at least the reasons set forth below.

Applicants have amended independent Claims 1, 48 and 51 recite, in part, a closed supporting container comprising an interior surface comprising an ethylene vinyl acetate copolymer. The amendments are supported in the specification, for example, at page 7, lines 1-25. Applicants have surprisingly found that providing an interior surface of a portion of the side walls constructed from an ethylene vinyl acetate covered by a fibrin matrix presents an environment conducive to adherent cell proliferation and maturation. For example, the flexible, gas permeable container is suitable for culturing anchorage dependent mammalian cells for expansion and transplantation, which has previously been done using rigid, gas impermeable cell culture flasks or plates. In contrast, Applicants respectfully submit that the skilled artisan would have no reason to combine the cited references to arrive at the present claims and, even if combinable, the cited references fail to disclose or suggest every element of the present claims.

Applicants respectfully submit that the skilled artisan would have no reason to combine the cited references to arrive at the claimed invention because the cited references have different modes of operation that teach away from each other and/or the present claims. For example, *Toner* is entirely directed to a modular cell culturing device including one or more two-compartment cartridges. See, *Toner*, column 2, lines 35-50. A polymeric membrane 30 (which may be coated with fibrin) separates a liquid compartment and an oxygenated fluid compartment of the cartridge. The cartridge entirely comprises rigid and impermeable exterior walls 50, which explicitly teaches away from the present claims. See, *Toner*, column 2, lines 39-45, column 7, lines 38-59, column 11, lines 27-41 ("rigid impermeable walls 50"). In fact, the walls of the cartridges are specifically intended and designed for being impermeable to liquids and gases to adequately maintain the bioreactor. See, *Toner*, column 7, lines 54-63.

Although *Toner* teaches using fibrin as a coating matter, the Patent Office's reliance on one aspect of *Toner*, which is already known in the art, while ignoring other teaching away aspects of *Toner* is a strong indication that the Patent Office is using Applicants' disclosure as a blueprint to pick and choose from isolated portions of the prior art in order to deprecate Applicants' claims. Such conduct is exemplary of hindsighted reasoning, which is clearly improper. Moreover, *Toner's* use of fibrin is specific to his device. For example, *Toner* does not coat the exterior rigid walls, but the intermediate separating membrane within the cartridge. As a result, the cells growth takes place on the intermediate membrane and not on the interior of the outer walls.

Smith is entirely directed to a multi-layer, flexible, gas-permeable container. See, *Smith*, column 2, lines 24-32. In fact, the outer walls that make up the container of *Smith* are made of the flexible, gas-permeable materials. *Smith* teaches that any cell growth takes place on the interior first and second flexible side walls. See, *Smith*, column 7, lines 7-9. Because *Smith* discloses a multi-layer flexible, gas permeable container, *Smith* explicitly teaches away from the impermeable and rigid multi-compartment cartridge taught by *Toner*. Moreover, *Toner's* use of the intermediate membrane for cell growth would lead the skilled artisan away from using the exterior walls for cell growth as taught by *Smith*.

If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims prima facie obvious. *In re Ratti*, 270 F.2d 810, 123 USPQ 349

(CCPA 1959). This certainly applies here where one of the cited references is directed to a cartridge entirely comprising a rigid and impermeable exterior walls (*Toner*) and the other cited reference is directed to a flexible, gas-permeable container (*Smith*). As a result, the principle of operation for each device is important and specific to that particular device. The Patent Office has provided no evidence that the device of *Smith* works as modified by *Toner* and vice versa. Moreover, because of these differences, one skilled in the art would not be motivated to modify or combine *Toner* and *Smith* to arrive at the present claims.

Toner also teaches away from a closed container as recited in the present claims. Instead, *Toner* is entirely directed to an open or flow-through cell-culturing device. See, *Toner*, column 2, lines 35-50. *Toner's* cartridge includes oxygenated fluid inlet/out 3,3' and liquid inlet/outlet 5,5'. The inlets and outlets permit continuous fluid flow through *Toner's* cartridge. The inlets and outlets fulfill an objective of *Toner*, which is to cultivate cells on membrane 30 by passing flowing fluid along each side of the membrane 30. See, *Toner*, column 2, lines 35-45. Accordingly, *Toner's* flow-through cartridge is an open system, not a closed system. *Toner's* open, flow-through cell-culturing device therefore teaches away from the closed support container recited in the present claims.

In addition, *Delmotte* teaches away from the present claims and a combination with *Smith* and *Toner*. For example, *Delmotte* teaches away from a closed support container having flexible and gas permeable exterior sidewalls in accordance with the present claims. *Delmotte* discloses a fibrin delivery device 10 having first and second syringes 12, 14 and a spray unit 18. A pressurizer 22 travels through each syringe 12, 14 to push fluid present in each syringe through the spray unit 18. *Delmotte*, column 8, lines 31-43, column 9, lines 47-58, Figures 1 and 4. One of ordinary skill in the art would recognize that syringes 12, 14 are rigid in order to withstand the pressure imposed by pressurizer 22 when pushing fluid out of each syringe. Moreover, *Delmotte's* rigid syringes teach away from the flexible container of *Smith* and the modular cell culturing device of *Toner*.

Applicants also respectfully submit that, even if combinable, the cited references do not disclose or suggest all of the claimed elements. For example, *Smith* fails to disclose or suggest a closed supporting container comprising an interior surface comprising an ethylene vinyl acetate copolymer as required, in part, by Claims 1, 48 and 51. Instead, *Smith* is entirely directed to an interior cell growth layer composed of polystyrene and exterior layer composed of a polymeric

layer comprising a multiple component polymer alloy blend containing styrene and diene copolymers and/or styrene and alpha-olefin copolymers. See, *Smith*, column 3, line 59 to column 4, line 10. Moreover, *Smith* explicitly teaches away from an interior surface comprising an ethylene vinyl acetate copolymer by stating:

> While EVA [ethylene vinyl acetate] can hold an electrostatic charge, the charge has the undesirable tendency to decay over time. Eventually, the decay of the charge on EVA will render the container ineffective for growing adherent cells. Rigid styrene flasks with an electrostatic charge are known, and show less of a tendency to lose charge over time.
>
> See, *Smith*, column 2, lines 7-12 (emphasis added).

Toner and *Delmotte* fail to remedy the deficiencies of *Smith*. For example, *Toner* and *Delmotte* also fail to disclose or suggest a closed supporting container comprising an interior surface comprising an ethylene vinyl acetate copolymer as required, in part, by Claims 1, 48 and 51. Moreover, although the Patent Office asserts that *Toner* is relied upon only for the teaching that a fibrin matrix may be used to accommodate cell growth, Applicants respectfully submit that *Toner* is merely cumulative with respect to the knowledge that fibrin may be used as a cell growth substrate. The ability of a fibrin matrix to support cell growth is known in the art. See, specification, page 3 line 23 to page 4 line 2 (coating a polymeric material with fibrin is known in the art). Nevertheless, the cited references fail to disclose or suggest the advantages of a fibrin matrix layer on a portion of the interior surface composed of an ethylene vinyl acetate copolymer in accordance with the present claims and provide no reasonable expectation of success with respect to same.

In sum, *Smith*, *Toner* and *Delmotte* fail to disclose or suggest any closed supporting container comprising an interior surface comprising an ethylene vinyl acetate copolymer and fail to even recognize the advantages, benefits and/or properties of such a container for the culture of cells in accordance with the present claims. For at least the reasons discussed above, the combinations of *Smith* and *Toner* or *Smith*, *Toner* and *Delmotte* are improper. Moreover, even if combinable, *Smith*, *Toner* and *Delmotte* do not teach, suggest, or even disclose all of the elements of independent Claims 1, 48 and 51 and the claims that depend from Claims 1, 48 and 51, and thus, fail to render the claimed subject matter obvious.

Accordingly, Applicants respectfully request that the obviousness rejections with respect to Claims 1-21 and 23-53 be reconsidered and the rejections be withdrawn.

For the foregoing reasons, Applicants respectfully request reconsideration of the above-identified patent application and earnestly solicit an early allowance of same.

Respectfully submitted,

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